

which is found in the compounds of the present invention in the 1-position. While the reference does teach such compounds containing an alkyl or alkenyl group, it is significant to note that the reference is clearly devoid of a teaching of the presence of a 1-cyclopropyl grouping. The Examiner has, apparently, recognized this deficiency in the primary reference and has attempted to reconstruct the present invention by a combination with Nakagome, et al. It is submitted that the combination is not warranted since there is no suggestion in Irikura, et al for the provision of compounds containing a 1-cyclopropyl group nor is there any suggestion in the secondary Nakagome, et al reference for the provision of compounds containing a 1-cyclopropyl group.

It is recognized that the secondary reference does refer to 1-alkyl, alkenyl and cycloalkyl groupings. However, the reference does not specify the 1-cyclopropyl group which is the one specifically involved in the present invention. Thus, since neither the primary nor secondary references applied by the Examiner teach compounds such as those of the present invention but containing a 1-cyclopropyl group, it is difficult to visualize how the reference can possibly be said to teach or suggest the cyclopropyl group when the references are considered in combination.

Under these circumstances, it is quite clear that the rejection which has been applied is without merit.

Apart from the above, note that in the instant application, page 12, lines 21 et seq., extensive experimental data is provided showing the unexpectedly outstanding results obtained using compounds containing the cyclopropyl grouping rather than compounds which contain in the 1-position an open chain alkyl grouping. In order to further emphasize this difference, there is included with this response a Declaration of Dr. Zeiler, co-inventor of the present application, which provides these data in verified form.

In view of the above, it is submitted that the rejection of claims 1-15 and 24-34 on the combination of Irikura, et al., with Nakagome, et al., is unwarranted and certainly no longer appropriate. Its withdrawal is expected.

Reconsideration is also requested of the rejection of claims 16-23 under 35 USC 103 as allegedly unpatentable over Matsumoto, et al. Here again, one is dealing with the provision of compounds which differ very substantially from those now being claimed. Note, in this connection, that the 1-substituent in the Matsumoto, et al., compounds, defined by the term  $R_1$ , must be an ethyl or vinyl group and neither are even closely related to the cyclopropyl substituent which must be found in the compounds of the present invention. Apart from the above, it is to be noted that

there is no procedure at all shown in Matsumoto, et al., to provide the 1-cyclopropyl compounds of the present invention.

Under these circumstances, it is submitted that the rejection of claims 16-23 on Matsumoto, et al is untenable and should be withdrawn.

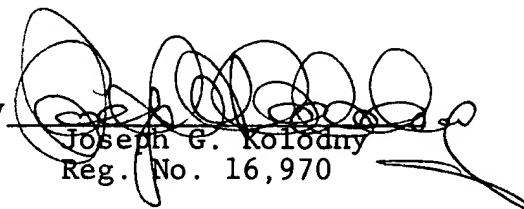
In accordance with an oral request from the Examiner, there is enclosed herewith a copy of J. Med. Chem. 1980, 23, 1358 (1980).

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Respectfully submitted,

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Encl. Declaration of Dr. Zeiler  
J. Med. Chem. 1980, 23, 1358  
Petition for Extension of Time in duplicate for  
2nd month (\$150.00).